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Emerging techniques for manipulating endocrine function in animal production: A comprehensive review

Muzemil Abdulazeez [1] and Abdulrasheed Buhari[2]

1. Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ilorin Kwara State Nigeria. **2.** Department of Veterinary Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Ilorin Kwara State Nigeria.

Abdulazeez, M. ORCID ID: 0009-0006-3004-5025; Buhari, A. ORCID ID: 0009-0001-7447-0131

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ABSTRACT

The endocrine system plays an important role in regulating various physiological processes in animals, encompassing growth, reproduction, metabolism, immune response, and overall homeostasis. This review delves into the fundamental definition and profound significance of endocrine function in animals, shedding light on its complex mechanisms and the vital role it plays in maintaining health and optimizing various aspects of animal production.

Keywords: endocrine glands, growth promoter, reproduction, hormones, endocrine disruptive chemicals.

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Introduction

The endocrine system, a complex network of glands and organs, is responsible for the secretion of hormones – vital molecules that govern a multitude of bodily functions. These functions encompass growth and development, metabolic processes, electrolyte balances, and reproduction (Nagy and Malcomson, 2022). This complex system comprises several key components, including the hypothalamus, pituitary gland, adrenal glands, gonads (testes and ovaries), thyroid gland, parathyroid glands, pancreas, and thymus (Skórka-Majewicz et al., 2020). Hormones, important to this system, are released into the bloodstream in response to specific triggers, reaching their target cells to convey critical messages (Nagy and Malcomson, 2022).

The endocrine system maintains a vigilant watch over the hormone levels in the blood, expertly regulating their release through complex biochemical mechanisms and the feedback loop (Hackney and Lane, 2015). Examples of these complex feedback loops are the hypothalamus-pituitary axis and the pituitary-adrenal axis, which finely tune hormone production and release (Paragliola et al., 2017). This complex system is instrumental in overseeing growth and development, tissue function, metabolism, and reproductive processes (Barzilai et al., 2012).

Undoubtedly, manipulating endocrine processes holds considerable potential in the realm of animal production. The significance of endocrines in the extents of nutrition, breeding, and overall production of farm animals cannot be overstated (Velazquez et al., 2008). The manipulation of endocrine processes promises enhanced animal growth, reproductive outcomes, and overall health. This can be achieved through a variety of strategies, including the administration of growth hormones as growth promoters, estrous synchronization, augmentation of milk production, the regulation of immune function to bolster health, and the reduction of stress by modulating cortisol levels. Such manipulation presents

*Corresponding Author: Abdulazeez Muzemil
E-mail: Muzammilabdulazeez@gmail.com.

a nuanced approach to optimizing animal production, aligning with the sophisticated science of endocrine function.

Endocrine regulation of growth and reproduction

Overview of key endocrine glands and hormones involved in growth and reproduction

The endocrine system, often referred to as the hormone system, is a fundamental component found across the animal kingdom, encompassing mammals, birds, fish, and numerous other species. This complex system comprises an array of glands distributed throughout the body, each with its specific function. These glands produce hormones, which are subsequently released into the bloodstream or the fluid surrounding cells. These hormones act as messengers, and their actions are recognized and responded to by receptors in various organs and tissues (Jameson, 2015). In essence, hormones function as the body's communication network, transmitting vital messages from one part of the body to another (Pert, 1988).

The endocrine system plays a important role in regulating an extensive spectrum of biological processes, from the earliest stages of life, through adulthood, and into old age. Its influence extends to the development of the brain and nervous system, the growth and function of the reproductive system, and the complex control of metabolism and blood sugar levels (Jameson, 2015).

Among the key players in this system are: Pituitary Gland: Often termed the "master gland," the pituitary gland exerts control over various other endocrine glands. It produces a plethora of hormones, including growth hormone, which fosters the growth of bones and other bodily tissues. Furthermore, it plays a crucial role in nutrient and mineral utilization. Additionally, the pituitary gland produces luteinizing hormone and follicle-stimulating hormone, which regulate the production of sex hormones – estrogen in females and testosterone in males, and also govern the production of eggs in females and sperm in males (Bharati et al., 2023).

Thyroid gland: The thyroid gland is responsible for the production of thyroid hormones. These hormones wield influence over all cells within the body and hold sway over biological processes such as growth, reproduction, development, and metabolism (Jameson, 2015).

Adrenal glands: These remarkable glands synthesize several hormones, including aldosterone, which maintains salt and water balance and blood pressure regulation. Furthermore, cortisol, produced by the adrenal glands, governs metabolism, influencing growth, maturation, and immune function (Nagy and Malcomson, 2022).

Pancreas: Serving as an exocrine and endocrine gland, the pancreas primarily focuses on controlling blood sugar levels. It achieves this through the production of insulin and glucagon (Knight, 2021).

Ovaries: In female animals, the ovaries are the primary source of sex hormones, including estrogen and progesterone. These hormones play a important role in regulating the estrous cycle, and they are key actors in processes such as pregnancy and parturition (Persson, 2000).

Testes: In males, the testes serve as the primary source of sex hormones, particularly testosterone. This hormone is instrumental in the development of male sex organs and the emergence of secondary sex characteristics (Toppari et al., 1996).

In addition to these primary actors, a host of other hormones are involved in the complex web of growth and reproduction. This includes hormones like growth hormone-releasing hormone, thyrotropin-releasing hormone, corticotropin-releasing hormone, gonadotropin-releasing hormone, oxytocin, vasopressin, dopamine, and somatostatin (Nagy and Malcomson, 2022). Each of these hormones, glands, and their functions, contribute to the awe-inspiring symphony that is the endocrine system, underscoring its indelible impact on the biological processes that shape life in the animal kingdom.

Hormonal interactions and pathways regulating growth and reproduction

The endocrine system is complex and involves a network of hormones and pathways that work together to ensure proper growth and reproductive function. Hormonal interactions and pathways play a crucial role in regulating growth and reproduction in animals. Here are some key points about the hormonal regulation of growth and reproduction:

1. Hormones regulating growth*:* Growth Hormone (GH): Produced by the pituitary gland, GH promotes protein synthesis throughout the body, especially in cartilage, bone, and muscle (Isaksson et al., 1985)

Somatotropin: A hormone produced by the pituitary gland, somatotropin is responsible for promoting protein synthesis and growth (Isaksson et al., 1985) .

Steroid sex hormones: Testosterone and estrogen also have a role in regulating growth in humans. The hormone surge during adolescence produces a growth spurt in both male and female animals (Rogol et al., 2002)

2. Hormones regulating reproduction: Gonadotropin-Releasing Hormone (GnRH): Released by the hypothalamus, GnRH stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary, which are essential for reproductive processes (Yaron and Levavi-Sivan, 2011)

Follicle-Stimulating Hormone (FSH): Produced by the anterior pituitary, FSH stimulates the growth and development of ovarian follicles in females and sperm production in males (Chappel and Howles, 1991) Luteinizing Hormone (LH): Also produced by the anterior pituitary, LH triggers ovulation in females and stimulates testosterone production in males (Chappel and Howles, 1991)

Sex Steroid Hormones: Estrogen and progesterone in females, and testosterone in males, play crucial roles in regulating reproductive processes, including the development of secondary sex characteristics and the regulation of gonad function (McEwen, 1992).

3. Interactions and pathways

Growth hormone and reproduction: There is evidence to suggest that growth hormone (GH) also directly modulates reproduction, exerting both gonadotropin-dependent and gonadotropin-independent effects (Hull and Harvey, 2014).

GH-insulin-like growth factor (IGF)-1-gonadal axis: This axis plays a significant role in reproduction, with GH and IGF-1 influencing gonadal function and the production of sex steroid hormones (Dosouto et al., 2019).

Hormonal control of animal performance: Hormones, including growth hormone and cortisol, interact and impact the development and performance of animals, particularly during niche shifts and metamorphosis (McCormick and Romero, 2017).

Manipulation of growth hormones

Exogenous administration of growth-promoting hormones

The practice of administering exogenous growth-promoting hormones is a widespread strategy in animal production, aimed at augmenting growth rates and enhancing feed efficiency (Qaid and Abdoun, 2022). These hormones encompass androgens, estrogens, glucocorticoids, progestogens, and synthetic compounds like trenbolone acetate and zeranol (Yazdan et al., 2022). It's noteworthy that the Food and Drug Administration (FDA) in the United States has sanctioned the utilization of these hormones in animal production (Qaid and Abdoun, 2022).

Exogenous administration of growth hormone to animals has far-reaching consequences, impacting various physiological processes, including growth and lactation (Peel et al., 1983). The key hormonal substances employed for growth promotion encompass naturally occurring steroids such as estradiol-17β, progesterone, and testosterone, alongside synthetic compounds like zeranol, trenbolone acetate, and melengestrol acetate (MGA) (Jeong et al., 2013). Nevertheless, the application of growth-promoting hormones has stirred debate concerning the safety of livestock products for human consumption. Despite the ongoing controversy, several countries routinely employ these hormones, concurrently reducing greenhouse gas emissions, energy use, water consumption, and reactive nitrogen loss in beef production compared to hormone-free methods (Skoupá et al., 2022). In the context of an evolving demand for sustainability, growth-promoting hormones hold the potential to enhance production efficiency, thereby contributing significantly to the overarching goal of producing more food with fewer resources (Hume et al., 2011).

Effects of growth hormone manipulation on growth rates and body composition: Growth hormone manipulation wields substantial influence over the growth rates and body composition of animals. Notably, most insights into GH's mode of action have been gleaned from laboratory rather than farm animals (Berryman et al., 2008). Additionally, the precise mechanisms underpinning GH's effects on metabolism remain a subject of ongoing inquiry (Chaves et al., 2013).

1. Effects on growth rates: Pituitary growth hormone (GH) emerges as a potent anabolic agent in animal production, exemplified by swifter growth rates and reduced feed consumption per unit of body weight gain in treated animals, alongside diminished carcass fat compared to untreated counterparts (Williams et al., 1994). The consequential impact on body composition is a product of GH's dichotomous effects on lean and fat mass – promoting the former while curtailing the latter (Palmer et al., 2009).

2. Effects on body composition: GH exercises a profound lipolytic effect, resulting in the reduction of adipose tissue mass, all while preserving lean body mass (Berryman and List, 2017). GH's effects are mediated either directly or through the induction of IGF-1, which governs overall body growth (Oberbauer, 2015). This hormone also drives the growth of lean tissue while curbing the accumulation of adipose tissue (Berryman and List, 2017). It's imperative to acknowledge that the dietary conditions to which animals are exposed assume a important role when assessing the effects of hormonal manipulation on body weight and adiposity in whole-animal models (Ribaroff et al., 2017).

Ethical and safety considerations of using growth hormones in animal production

The utilization of growth hormones in animal production gives rise to ethical and safety concerns that warrant attention.

1. Ethical considerations: From an animal welfare perspective, the application of growth hormones can inflict discomfort and pain on animals, potentially leading to health problems like lameness and joint pain (Ormandy et al., 2011). The genetic modification of some growth hormones through genetic engineering further raises ethical concerns concerning animal welfare and potential risks to human health (Ormandy et al., 2011).

2. Safety considerations: In the context of human health, the use of hormonal substances in food-producing animals has been linked to potential health concerns, including an elevated risk of breast cancer and other health issues (Nachman and Smith, 2015). Moreover, the use of growth promoters, including antibiotics, can contribute to the emergence of resistance genes, rendering infections harder to treat in both animals and humans (Jeong et al., 2013). The presence of growth hormones in meat may pose potential health risks for consumers (Jeong et al., 2013).

Induction of superovulation and multiple pregnancies

The induction of superovulation and multiple pregnancies represents a vital technique in animal production, involving hormonal treatments to stimulate the recruitment and development of multiple follicles in animals, leading to the production of a larger number of embryos (González-Bulnes et al., 2004). This technique is frequently employed alongside embryo transfer to expedite the propagation of animals with desired genetic traits (Jainudeen et al., 2016). Follicle-stimulating hormone (FSH) stands as the most commonly used hormone for inducing superovulation, but the yield of embryos can be variable and influenced by factors such as breed, age, nutrition, and management practices (S. Khan et al., 2023). Quality variations in embryos produced through superovulation in cow have also been documented (S. U. Khan et al., 2022). Consequently, ongoing research endeavors aim to refine and simplify superovulation protocols. Selection of multiparous animals with high pregnancy experience and consideration of ovarian follicular development activity may enhance the outcomes of simplified superovulation (Khan et al, 2022).

Inducing multiple pregnancies is a sought-after outcome of superovulation in animal production, facilitating the generation of a larger number of offspring harboring desirable genetic traits (Moore and Thatcher, 2006). In cattle raised for beef production, the induction of twin pregnancies holds particular significance.

Thyroid hormone manipulation

Influence of thyroid hormones on metabolism and growth

Thyroid hormones have a critical role in animal metabolism, growth, and development. Altering thyroid hormone levels in animal production can significantly impact growth and metabolism, as these hormones are fundamental for normal growth and development. Thyroid hormone supplementation has been demonstrated to increase growth rates in animals (Todini, 2007). Conversely, a deficiency in thyroid hormones can lead to growth retardation and reduced productivity (Choksi et al., 2003). Additionally, thyroid hormones are important in regulating animal metabolism. They elevate the metabolic rate, resulting in increased energy expenditure and heat production (Bianco et al., 2005). Manipulating thyroid hormones can thus influence the energy balance of animals and, in turn, impact their productivity.

In terms of reproduction, thyroid hormones also play a role. Studies have shown that thyroid hormone deficiency can lead to reproductive issues in animals, including reduced fertility and litter size (Choksi et al., 2003). Supplementation of thyroid hormones can enhance reproductive performance in animals. Moreover, maternal thyroid hormone levels during pregnancy and lactation can influence offspring growth and development. Studies have indicated that maternal thyroid hormone supplementation can increase offspring growth rates and enhance their survival (Hsu et al., 2022).

Stress hormone regulation and animal welfare

Stress hormones can have profound effects on animal well-being and productivity. Chronic stress can lead to severe health problems, reduced productivity, and behavioral changes (Ghassemi Nejad et al., 2022). Stress can result in decreased growth, impaired reproductive success, and compromised cognitive abilities (Martínez-Miró et al., 2016). In livestock, stress can increase mortality and morbidity, decrease growth efficiency, and lead to less desirable end products (Edwards, 2010). To effectively manage the consequences of stress in animals, it is crucial to assess the level of stress, identify stressors, and consider various factors that affect the stress response (Ghassemi Nejad et al., 2022).

Hormones involved in stress responses can lead to physiological and behavioral changes in animals (Tilbrook and Ralph, 2018). Various biomarkers are employed to evaluate stress, categorized into four groups based on the physiological system or axis assessed: the sympathetic nervous system, the hypothalamic-pituitary-adrenal axis, the hypothalamic-pituitary-gonadal axis, and the immune system (Martínez-Miró et al., 2016).

Strategies to minimize stress-related hormonal responses in animal production

There are several strategies that can be implemented to minimize stress-related hormonal responses in animal production, enhancing both animal health and productivity:

Environmental Modifications: Providing animals with a comfortable environment, including proper ventilation, temperature control, and sufficient space, can reduce stress (Collier et al., 2006).

Nutritional Management: Ensuring animals receive a balanced diet with adequate nutrients can lower stress, as nutritional deficiencies can lead to increased stress and reduced productivity (West, 1999).

Handling and Management Practices: Proper handling and management practices that minimize stressors, reduce noise levels, and provide a calm and quiet environment can help alleviate stress in animals (Lloyd, 2017).

Genetic Selection: Selecting animals with calm temperaments that are less susceptible to stress can contribute to reduced stress-related hormonal responses (Chen et al., 2015).

Health Management: Implementing proper health management practices, such as regular vaccinations, parasite control, and timely treatment of sick animals, can minimize stress (Pertanika and Trop, 2018).

Behavioral Enrichment: Providing opportunities for natural behaviors through environmental enrichment, socialization, and access to toys can reduce stress in animals (Maria Dimova and Stirk, 2019).

Supplementation: The supplementation of specific nutrients, such as chromium, can help alleviate stress in animals (El-Kholy et al., 2017).

Heat Stress Management: In hot climates, providing shade, cooling systems, and access to cool water can help mitigate heat stress in livestock production systems (Dourmad et al., 2022).

Balancing productivity goals with animal welfare concerns

Balancing productivity goals with animal welfare concerns under hormone manipulation in animal production is a complex and multifaceted challenge. Although hormones are often used to enhance productivity, their use can have both positive and negative effects on animal welfare. It is essential to recognize that while animals require a minimum level of care to be productive, productivity does not automatically equate to good welfare (Lusk and Norwood, 2011). Animal welfare cannot be solely determined by productivity; it encompasses various aspects of an animal's overall well-being (Fraser, 1995).

Management practices play a critical role in enhancing both animal welfare and productivity. However, the impact of these practices on livestock performance can vary depending on factors such as species, environment, and specific management protocols (Morgado et al., 2023). It is also essential to consider the individual needs and requirements of animals to achieve a balanced approach.

Efforts to increase productivity while reducing greenhouse gas emissions per unit of product are in line with goals set by organizations like the World Bank (Laborde et al., 2021). This dual focus on welfare and productivity is particularly relevant in the dairy industry, where farmers aim to boost productivity using fewer resources (Oltenacu and Algers, 2005). Additionally, animal welfare in extensive production systems is an ongoing area of concern, with research primarily focusing on welfare issues commonly associated with intensive systems (Temple and Manteca, 2020).

Hormonal manipulation in aquaculture

Aquaculture, the cultivation of aquatic organisms like fish, crustaceans, mollusks, and aquatic plants, frequently employs hormonal manipulation techniques to regulate reproductive functions in captive fish. The use of hormones is vital for sustaining commercial aquaculture production. The fish reproductive cycle is separated into the growth (gametogenesis) and maturation phase (oocyte maturation and spermiation), both controlled by the reproductive hormones of the brain, pituitary, and gonad (Mylonas et al., 2010).Hormonal manipulations of reproductive function in cultured fishes have focused on the use of either exogenous luteinizing hormone (LH) preparations that act directly at the level of the gonad, or synthetic agonists of gonadotropin-releasing hormone (GnRHa) that act at the level of the pituitary to induce release of the endogenous LH stores (Mylonas et al., 2010). Hormones are used in fish farming to increase fish production when one sex of a species has the capacity to grow bigger and faster than the other sex (Hoga et al., 2018).

For successful aquaculture, determination of the reproductive condition of captive broodstock is important for administering hormonal therapies and inducing spawning (Mylonas et al., 2010). The first step for hormone-induced spawning is to determine the type of hormone suitable for the fish species of interest (Chatakondi et al., 2018). Efficacy of hormones is determined by the dose and timing of administration (Chatakondi et al., 2018). The use of hormones in aquaculture has been studied extensively, and analytical methods have been developed to determine their residues (Hoga et al., 2018). The first methods employed freshly ground pituitaries collected from reproductively mature fish, which contained gonadotropins (mainly LH) (Zohar and Mylonas, 2001). Hormonal manipulation is an important key factor for the sustainability of commercial aquaculture production of wild captive fish (Mylonas et al., 2010).

Hormonal control of sex differentiation

Sex differentiation in fish and other aquatic species is influenced by a combination of genetic, physiological, and environmental factors. Hormones, particularly gonadotropins from the pituitary gland, play a significant role in regulating gonadal development and differentiation in some fish species (Arcand-Hoy and Benson, 1998). Environmental factors, such as temperature, can interact with hormonal cues to influence sex determination (Budd et al., 2015).

Hormonal sex reversal treatments, utilizing exogenous hormones and other chemicals, have been applied to many fish species. These treatments enable changes in an individual's sex and are particularly useful in aquaculture (Piferrer, 2001). Aromatase and estrogens have been identified as key components in the process of sex differentiation in fish (Guiguen et al., 2010).

Hormone-assisted breeding techniques in aquaculture

Hormone-assisted breeding techniques are widely utilized in aquaculture to increase fish production and enhance the quality of offspring. These techniques involve administering hormones to fish for various purposes, including:

Inducing and sustaining vitellogenesis: To stimulate egg production, hormones like estrogens are employed.

Sex reversal: Hormones can be used to change the sex of fish to favor more productive sexes.

Chromosome Set Manipulation: Hormones can be used to manipulate the chromosome set in fish to generate desired characteristics or traits.

Hybridization: Hormones are used to facilitate the hybridization of different fish species to create new varieties or species (Mylonas et al., 2010).

For example, European eel aquaculture aims to close the life cycle in captivity, overcoming natural inhibitions to sexual maturation in both sexes by applying assisted reproduction protocols (Benini et al., 2022). Studies continually investigate the efficacy of various synthetic hormones in inducing breeding in different fish species, striving to improve the efficiency of hormone-assisted breeding techniques and ensure high-quality offspring (Nazir et al., 2023).

Environmental considerations and challenges in hormone use in aquaculture

The use of hormones in aquaculture comes with various environmental considerations and challenges:

Eutrophication: Aquaculture effluents with high biological oxygen demand (BOD) and suspended solids can contribute to eutrophication, characterized by excessive growth of algae and aquatic plants, which can lead to oxygen depletion and fish mortality (Hlordzi et al., 2020).

Accumulation of waste products: Aquaculture generates waste products, including uneaten food and feces, which can accumulate in the environment and affect water quality (Fraga-Corral et al., 2022).

Release of Chemicals: The widespread use of bioactive compounds, such as hormones, raises concerns about their release into the aquatic environment (Okeke et al., 2022).

Water quality concerns: Specific environmental steroids are a significant concern for water quality due to their potential adverse effects on aquatic organisms (Agrawal et al., 2010).

Biosafety concerns: The use of advanced biotechnological tools like CRISPR/Cas in fish aquaculture introduces biosafety concerns related to gene flow to wild populations and potential unintended effects on non-target organisms (Bohua et al., 2023).

Balancing the benefits of aquaculture with these environmental concerns requires careful management, regulation, and the development of sustainable and environmentally friendly practices in the industry.

Endocrine disruptors and unintended effects

Introduction to endocrine-disrupting compounds (EDCs)

Endocrine-disrupting compounds (EDCs) are natural or human-made chemicals that may mimic, block, or interfere with the body’s hormones, which are part of the endocrine system (Crawford et al., 2017). EDCs can be found in the environment, food sources, personal care products, and manufactured products (Archer et al., 2017). Exposure to EDCs can occur through diet, air, skin, and water (Metcalfe et al., 2022). The endocrine system is a network of glands and organs that produce, store, and secrete hormones, which regulate the body's healthy development and function throughout life (Nagy and Malcomson, 2022).

EDCs can interfere with the normal function of the endocrine system by acting like "hormone mimics" and tricking the body into thinking that they are hormones, blocking natural hormones from doing their job, increasing or decreasing the levels of hormones in the blood, or changing how sensitive the body is to different hormones (Uthayanan and Sundareswaran, 2023). According to the Endocrine Society, there are nearly 85,000 human-made chemicals in the world, and 1,000 or more of those could be endocrine disruptors, based on their unique properties (Nagy and Malcomson, 2022). EDCs are associated with a wide array of health issues, including male reproductive problems, early female puberty, leukemia, brain cancer, and neurobehavioral disorders (Gore et al., 2014). Research is ongoing to better understand how EDCs work and define their role in health and disease. Research areas in progress include developing new models and tools to better understand how EDCs work, developing and applying high throughput assays to identify substances with endocrine disrupting activity, conducting animal and human health research to define linkages between exposure to EDCs and health effects, developing new assessments and biomarkers of exposure and toxicity, and identifying and developing new (Crews and Mclachlan, 2006).

The Endocrine Society and International POPs (Persistent Organic Pollutant) Elimination Network (IPEN) have joined together to develop an EDC Guide to raise global awareness about EDCs. The guide draws from each organization's strengths to present a more comprehensive picture of global EDC exposures and health risks than either could have done alone. Endocrine Society authors contributed the scientific and health-related content (Gore et al., 2014).

Potential risks of EDCs in animal production and the food chain

Endocrine Disruptive Chemicals (EDCs) are a group of chemicals that can interfere with the endocrine system, which is responsible for regulating hormones in the body. EDCs can have a significant impact on animal production and the food chain, as they can enter the food chain through various routes, including the living environment of food-producing organisms, direct use in food production, and release from food contact materials (Mantovani, 2016).

Here are some potential risks of EDCs in animal production and the food chain:

Reproductive and developmental effects: EDCs can interfere with the reproductive and developmental systems of animals, leading to reduced fertility, birth defects, and other reproductive problems (Mallozzi et al., 2016).

Hormonal imbalances: EDCs can disrupt the normal functioning of hormones in animals, leading to hormonal imbalances that can affect various body systems (Lee et al., 2013).

Cancer: Some EDCs have been linked to an increased risk of cancer in animals (Alsen et al., 2021).

Immune system effects: EDCs can weaken the immune system of animals, making them more susceptible to diseases and infections (Ansar Ahmed, 2000).

Environmental effects: EDCs can have a significant impact on the environment, as they can accumulate in soil, water, and air, and can affect wildlife and ecosystems (Kabir et al., 2015).

Human health effects: EDCs can also have an impact on human health, as they can enter the human body through the food chain and other routes of exposure. Some EDCs have been linked to an increased risk of various health problems, including cancer, reproductive problems, and developmental disorders (Yilmaz et al., 2020).

Strategies to mitigate the exposure and effects of endocrine disruptors

Endocrine disruptors are synthetic chemicals found in everyday products like plastics and fragrances that can mimic hormones and interfere with the delicate endocrine system. Exposure to these chemicals can cause irreversible changes in the body, especially during phases of accelerated development like in utero and throughout the developmental period (Mallozzi et al., 2016). To mitigate the risks of EDCs in animal production and the food chain, it is important to take steps to reduce exposure to these chemicals. This can include using alternative methods of pest control, reducing the use of plastics and other materials that contain EDCs, and improving waste management practices to prevent the release of EDCs into the environment (Campbell et al., 2006).

Emerging technologies in endocrine manipulation

Advances in genetic and biotechnological approaches for hormone manipulation

Advances in genetic and biotechnological approaches have been used to manipulate hormones in animal production. Here are some ways in which these approaches have been used:

1. Genetic engineering: Scientists have used genetic engineering to create transgenic animals that express higher levels of growth hormone, which can increase productivity in farm animal species (Ormandy et al., 2011). For example, transgenic pigs and sheep have been genetically altered to express higher levels of growth hormone (Devlin et al., 2009).

2. Gene knock-out techniques: Gene knock-out techniques have been used to create designer companion animals. For example, some companies use genetic engineering techniques to remove the gene that codes for the major cat allergen Fel d1, creating hypoallergenic cats (Ormandy et al., 2011).

3. Modification of animal products: Modern biotechnological techniques have been used to alter the characteristics of animal products. For example, genetic manipulation in transgenic animals can alter the carcass to be lower in fat and cholesterol (Asaye et al., 2014).

4. Improved milk production traits: Genetic engineering and cloning have been used to improve milk production in livestock. Scientists hope to produce animals with altered traits such as milk composition (Moore and Thatcher, 2006). For example, a transgenic goat has a transgene that codes for a human protein under the control of a promoter region that targets expression specifically to the mammary gland. The human protein is secreted in the goat's milk but nowhere else in the animal (Pittius et al., 1988).

While these approaches have shown promise in improving animal productivity and food quality, there are also ethical and welfare concerns associated with genetic engineering of animals (Ormandy et al., 2011). The generation of a new genetically engineered line of animals often involves the sacrifice of some animals and surgical procedures on others (Ormandy et al., 2011). Therefore, it is important to consider the welfare of the animals involved in these processes.

Gene editing and its potential applications in altering endocrine functions

Gene editing is a powerful tool that allows for precise and efficient alteration of an animal's DNA (McFarlane et al., 2019). By using gene editing technology, targeted mutations can be made in specific genes, and novel lines of animals with valuable phenotypes can be produced (Li et al., 2020). Gene editing combined with animal production technologies provides the potential for accelerating the genetic improvement of livestock, including the alteration of production traits, enhancing resistance to disease, reducing the threat of zoonotic disease transmission, and improvement of livestock welfare (Perisse et al., 2021).

Endocrine functions play a crucial role in animal production, and gene editing can be used to alter these functions to improve livestock productivity. Here are some potential applications of gene editing in altering endocrine functions in animal production:

1. Improving growth and muscle development: The myostatin gene (MSTN) is a common target for research into increased growth and muscle development. Gene editing can be used to inactivate the MSTN gene, leading to increased muscle mass and improved meat quality (Zhao et al., 2022).

2. Enhancing milk production: Gene editing can be used to alter the genes responsible for milk production, leading to increased milk yield and improved milk quality (Kadarmideen et al., 2003).

3. Reducing stress and improving animal welfare: Gene editing can be used to alter the genes responsible for the stress response in animals, leading to reduced stress and improved animal welfare (Kramer and Meijboom, 2021).

4. Improving reproductive performance: Gene editing can be used to alter the genes responsible for reproductive performance in animals, leading to improved fertility and increased litter size (Abdoli et al., 2016).

Future prospects of precision endocrinology in animal production:

Precision endocrinology is a rapidly growing field in animal production that aims to improve animal health, welfare, and productivity by using precise measurements of hormones and other biomarkers. Here are some future prospects of precision endocrinology in animal production:

1. Improved reproductive management: Reproductive hormones play a crucial role in animal reproduction, and precise measurements of these hormones can help improve reproductive management in livestock. For example, measuring progesterone levels in dairy cows can help identify the optimal time for insemination, leading to improved conception rates and reduced calving intervals (Crowe et al., 2018).

2. Better growth and feed efficiency: Hormones such as growth hormone and insulin-like growth factor (IGF-1) are important regulators of growth and metabolism in animals. Precise measurements of these hormones can help identify animals with superior growth and feed efficiency, allowing farmers to select and breed animals with desirable traits (Velazquez et al., 2008).

3. Improved animal welfare: Hormones such as cortisol and oxytocin are indicators of stress and social bonding, respectively, in animals. Precise measurements of these hormones can help identify animals that are experiencing stress or social isolation, allowing farmers to take corrective actions to improve animal welfare (Neethirajan et al., 2021).

4. Reduced use of antibiotics: Hormones such as cortisol and progesterone are also involved in the immune response of animals. Precise measurements of these hormones can help identify animals that are at risk of developing infections, allowing farmers to take preventive measures and reduce the need for antibiotics (Neethirajan and Kemp, 2021).

5. Integration with other precision livestock farming technologies: Precision endocrinology can be integrated with other precision livestock farming technologies such as precision feeding, precision health monitoring, and precision genetics to create a comprehensive (Tekın et al., 2021).

Regulatory and ethical considerations

International regulations and guidelines for the use of hormones in animal production

International regulations and guidelines for the use of hormones in animal production vary across different countries and regions. Here are some key points:

1. European union: In the European Union, the use of substances having a hormonal action for growth promotion in farm animals is prohibited (Serratosa et al., 2006).

2. United states: In the United States, the Food and Drug Administration (FDA) has approved the use of growth-promoting hormones such as estradiol, progesterone, testosterone, trenbolone acetate, and zeranol in beef cattle and sheep (Qaid and Abdoun, 2022). However, no steroid hormone implants are approved for growth purposes in dairy cows, veal calves, pigs, or poultry (Drouillard, 2018).

3. Benefits of hormone use: The use of hormonal active growth promoters ("hormones") in farm animals can increase the production of veal and beef significantly, up to 15% (Stephany et al., 2001). Research has demonstrated that hormone treatment improves growth rate, nitrogen retention, and feed conversion efficiency during the five- to six-week period before slaughter (Velle, W.1982).

4. Human health concerns: The former Scientific Committee on Veterinary Measures relating to Public Health (SCVPH) thoroughly re-evaluated the risks to human health from hormone residues in bovine meat and meat products treated with six hormones for growth promotion (Kesler, 1985). In 1999, this independent scientific advisory body concluded that no acceptable daily intake (ADI) could be established for any of these hormones (Alemanno and Capodieci, 2012).

5. Compliance with limits: The levels of hormone residues found in beef originating from the USA are, in the vast majority of cases, below the Maximum Residue Limit as recommended by the FAO/WHO Joint Expert Committee of Food Additives (Stephany et al., 2001). More than 20 countries use growth-promoting hormones regularly and have reduced greenhouse gas emissions, energy use, water use, and reactive nitrogen loss of beef production in comparison to beef raised without growth-promoting hormones (Di Benedetto et al., 2017).

In conclusion, the use of hormones in animal production is a complex issue that involves various factors such as regulations, health risks, and economic importance. While some countries have banned the use of hormones for growth promotion in farm animals, others have approved certain hormones under strict conditions. It is important to consider the potential risks and benefits of using hormones in animal production and to establish safe limits for hormone residues in meat to ensure consumer safety.

Ethical considerations regarding hormone use and animal welfare

Hormone use in animals can raise ethical concerns related to animal welfare. Here are some key considerations:

1. Proper treatment of experimental animals: To avoid undue suffering of animals, it is important to follow ethical considerations during animal studies (Festing and Wilkinson, 2007). This includes providing the best possible care to animals from both ethical and scientific points of view.

2. The "4 R's": The "4 R's" of animal research ethics refer to the principles of Replacement, Reduction, Refinement, and Responsibility (Osinubi, 2013). Responsibility refers to concerns around promoting animal welfare by improving experimental animals' social life, developing advanced scientific methods for objectively determining sentience, consciousness, experience of pain, and intelligence in the animal kingdom, as well as effective involvement in the professionalization of the public discussion on animal ethics (Kiani et al., 2022).

3. Clear rationale and reasoning: Researchers must have a clear rationale and reasoning for the use of animals in a research project. They must have a reasonable expectation of generating useful data from the proposed experiment, and the research study should be designed in such a way that it involves the lowest possible sample size of experimental animals while producing useful results (Kiani et al., 2022).

4. Genetic engineering: Genetic engineering of animals can raise ethical issues, including concerns for animal welfare (Ormandy et al., 2011). Governing bodies have started to develop relevant policies, often calling for increased vigilance and monitoring of potential animal welfare impacts (Ormandy et al., 2011).

5. Wild animal welfare: Research involving wild animals can also raise ethical concerns related to animal welfare (Soulsbury et al., 2020). It is important to consider the welfare of wild animals and the ethics of using them in scientific research (Soulsbury et al., 2020).

6. Guidelines for ethical conduct: The American Psychological Association (APA) has developed guidelines for ethical conduct in the care and use of nonhuman animals in research (Akins and Panicker, 2012). These guidelines are for psychologists working with nonhuman animals and are informed by Section 8.09 of the Ethical Principles of Psychologists and Code of Conduct (Behnke and Jones, 2012). The acquisition, care, housing, use, and disposition of nonhuman animals in research must comply with applicable federal, state, and local laws and regulations, institutional policies, and with international conventions to which the United States is a party (Behnke and Jones, 2012).

Consumer perceptions and attitudes towards hormone-treated animal products

Consumer perceptions and attitudes towards hormone -treated animal products are influenced by various factors, including animal welfare, health concerns, and ethical considerations.

1. Consumer attitudes: Consumer attitudes, subjective norms, and perceived behavioral control have significant and positive effects on their purchase intentions of animal welfare-friendly products (Chang and Chen, 2022).

2. Awareness of animal welfare: Consumers are aware of the pain animals experience in animal agriculture, and this awareness can influence their dietary choices (Fonseca and Sanchez-Sabate, 2022).

3. Health concerns: Study participants acknowledged that what was bad for the animals was ultimately bad for consumers, particularly in relation to the control of disease, and consumer negativity regarding the use of antibiotics in intensive production systems, with all being linked to human health concerns (Clark et al., 2016).

4. Animal welfare labels: Consumers who have greater concern for animal welfare consume animal products less frequently, purchase welfare-friendly products more frequently, and indicate a greater use of welfare-related labels (Clark et al., 2016).

Overall, consumers' perceptions and attitudes towards hormone-treated animal products are complex and influenced by various factors. Animal welfare, health concerns, and ethical considerations are some of the key factors that can influence consumer choices.

Case studies and success stories

Real-world examples of successful endocrine manipulation in animal production

1. Growth promotion: Hormones like estrogen, progesterone, and testosterone have been used to promote growth in beef cattle, dairy cows, and pigs. For instance, estrogenic compounds like diethylstilbestrol (DES) and hexoestrol have been shown to increase weight gain and feed efficiency in beef cattle. The use of testosterone implants in beef cattle has also increased muscle mass and reduced fat deposition (Reddy et al., 2014).

2. Reproductive management: Hormones play a crucial role in managing the reproductive processes of animals. Prostaglandins are used to synchronize estrus in dairy cows, while gonadotropins like follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are used to induce ovulation in mares and cows. Progesterone is used to suppress estrus in mares and synchronize estrus in beef cattle (Bó and Mapletoft, 2014).

3. Disease prevention: Hormones can be used to prevent diseases in animals. Melatonin has been shown to enhance the immune system and reduce the incidence of infectious diseases in sheep and cattle. Growth hormone has improved the immune response in chickens and reduced the incidence of infectious diseases (Leshchinsky and Klasing, 2001).

4. Transgenic animals: Transgenic animals are used to produce specific proteins or traits. Transgenic cows have been developed to produce human lactoferrin in their milk, which has potential applications in infant formula and other food products (Ã et al., 2006).

Comparative analysis of production outcomes using hormone manipulation techniques

1. DES implants: DES implants have been shown to result in an increase of about 12% in gain and an improvement in feed conversion efficiency (FCE) of approximately 10% in animals (Kling et al., 2012).

2. Glucocorticoid manipulation: Glucocorticoid manipulation has been used in survival studies of breeding black-legged kittiwakes (Crossin et al., 2016). However, there are concerns about the safety of hormonal application in farm animal production (Qaid and Abdoun, 2022).

3. Thyroid hormone manipulation: Differential effects of thyroid hormone manipulation and β adrenoceptor agonists have been studied (Mostyn et al., 2008).

In general, hormone manipulation techniques have been shown to improve production outcomes in animal production. However, safety concerns regarding hormonal application in farm animal production exist, and alternative methods to enhance animal production are being explored (Sillence, 2004).

Lessons learned and implications for future research and practice

Lessons learned

1. Genetic defects of protein folding in the secretory pathway can cause endocrine disorders in animals (Morishita and Arvan, 2021).
2. New evidence obtained in genetically manipulated research animals has challenged the old paradigm of the relationship between growth hormone and reproduction (Dosouto et al., 2019).
3. There are relationships between endocrine traits and life histories in wild animals, but there are also potential pitfalls in studying these traits (Dosouto et al., 2019).
4. A range of techniques allows analysis of the pituitary gland in awake mammalian models in unparalleled detail, complementing large-scale imaging studies (Hoa et al., 2019).
5. Epidemiology and animal experiments have often focused on male reproduction, testicular dysgenesis, and decreased fertility (Skakkebæk et al., 2001).

Implications for future research and practice

1. Researchers should continue to investigate the genetic basis of endocrine disorders in animals, particularly those caused by defects of protein folding in the secretory pathway (Zhu et al., 2002).
2. Future studies should consider the new evidence obtained in genetically manipulated research animals when examining the relationship between growth hormone and reproduction (Aubin-Horth and Renn, 2009).
3. Researchers should be aware of potential pitfalls when studying endocrine traits in wild animals and should take steps to mitigate these risks (Kavlock et al., 1996).
4. The range of techniques available for analyzing the pituitary gland in awake mammalian models should be further explored and developed (Hoa et al., 2019).
5. Future research on endocrine disruptors should consider the potential effects on male reproduction, testicular dysgenesis, and decreased fertility (Skakkebæk et al., 2001).

The lessons learned and implications for future research and practice underscore the need for continued investigation into the genetic and physiological basis of endocrine disorders, as well as the potential risks and benefits of manipulating endocrine systems in animals.

Conclusions and future directions

Key Findings

1. Successful Endocrine Manipulation Techniques: Endocrine manipulation techniques have been applied successfully in animal production. These include using hormones for growth promotion, reproductive management, disease prevention, and the development of transgenic animals to produce specific proteins or traits.

2. Production outcomes: The use of hormones like DES implants has led to increased weight gain and improved feed conversion efficiency in animals. However, there are concerns about the safety of hormonal applications in farm animal production, and alternative methods are being explored.

3. Lessons learned: Genetic defects in the secretory pathway can cause endocrine disorders in animals. New evidence from genetically manipulated research animals has challenged our understanding of the relationship between growth hormone and reproduction. Researchers should consider potential pitfalls when studying endocrine traits in wild animals.

Insights

1. Ethical considerations: The use of hormones in animal production raises ethical concerns related to animal welfare. Proper treatment of experimental animals, adherence to the "4 R's" of animal research ethics, and clear rationale for using animals in research are essential.

2. International regulations: Regulations regarding the use of hormones in animal production vary across different countries and regions. Some countries, like the European Union, prohibit the use of hormonal growth promoters, while others, like the United States, approve specific hormones under strict conditions. Consumer perceptions and attitudes are influenced by factors such as animal welfare, health concerns, and ethical considerations.

3. Precision endocrinology: Precision endocrinology offers promising prospects for improving animal health, welfare, and productivity through the precise measurement of hormones and biomarkers. It can enhance reproductive management, growth, and feed efficiency while reducing the use of antibiotics and improving animal welfare.

4. Health risks: Endocrine-disrupting compounds (EDCs) can interfere with the normal function of the endocrine system and are associated with various health issues, including reproductive problems, early puberty, cancer, and neurobehavioral disorders.

5. Future research: Future research should focus on investigating the genetic basis of endocrine disorders in animals, considering new evidence from genetically manipulated animals, and addressing the relationship between endocrine traits and life histories in wildlife. Additionally, researchers should explore advanced techniques for analyzing the pituitary gland in awake mammalian models.

In summary, the review highlights the successful applications of endocrine manipulation techniques in animal production, ethical considerations in using hormones, variations in international regulations, the role of precision endocrinology, health risks associated with endocrine-disrupting compounds, and the need for further research to understand and improve endocrine manipulation in animals.

This review on endocrine manipulation in animal production highlights several gaps in knowledge and areas for further research. Here are some of the key gaps and research needs:

1 Safety and long-term effects: While the review discusses the benefits of endocrine manipulation, there is a need for further research to comprehensively assess the long-term safety and potential adverse effects of using hormones and other endocrine-disrupting compounds (EDCs) in animal production. This includes studying the impact on animal health, meat quality, and the environment. Longitudinal studies on the health and welfare of animals exposed to hormone manipulation are necessary.

2. Alternative approaches: The review mentions that there are concerns about the safety of hormonal applications in animal production, which suggests a need for research into alternative approaches to achieve similar or improved production outcomes. Identifying and developing non-hormonal growth promoters and disease prevention methods is essential.

3. Consumer perception and behavior: Further research is needed to understand the factors influencing consumer perceptions and behaviors regarding hormone-treated animal products. This includes studying consumer attitudes toward animal welfare, health concerns, and ethical considerations. Additionally, research can explore the effectiveness of labeling and communication strategies in influencing consumer choices.

4. Ethical considerations: Research should continue to explore ethical considerations in using hormones in animal production. This includes refining ethical guidelines for the treatment of experimental animals, promoting the principles of Replacement, Reduction, Refinement, and Responsibility (the "4 R's"), and addressing concerns related to genetic engineering and research involving wild animals.

6. Genetic and molecular studies: To better understand endocrine disorders and the genetic basis of hormone-related traits, further research is needed to investigate genetic defects in the secretory pathway that can lead to endocrine disorders. This research could provide insights into endocrine-related health issues in animals.

6. Precision endocrinology: The review highlights the potential of precision endocrinology in improving animal health, welfare, and productivity. Future research should focus on developing and validating precise and non-invasive methods for measuring hormones and biomarkers in animals to enhance reproductive management, growth, and animal welfare.

7. Environmental impact: While the review briefly mentions the impact of endocrine manipulation on the environment, there is a need for comprehensive research on how the use of hormones and EDCs in animal production affects soil, water, air, and ecosystems. Studying the environmental risks and sustainability of these practices is crucial.

8. Global comparative analysis: Further research can involve conducting a global comparative analysis of regulations and practices related to hormone use in animal production. This would provide a more in-depth understanding of regional variations and their implications for international trade and consumer preferences.

9. Transgenic animal welfare: As the review mentions the development of transgenic animals, future research should focus on assessing the welfare and ethical considerations related to these genetically modified animals. This research can help establish ethical guidelines and best practices for using transgenic animals in animal production.

10 Health risks of endocrine-disrupting compounds: Research should continue to investigate the health risks associated with endocrine-disrupting compounds (EDCs), particularly their links to diseases such as cancer, reproductive problems, and neurobehavioral disorders. This includes conducting epidemiological studies to better understand the effects of EDC exposure on human and animal health.

In conclusion, this review highlights various knowledge gaps and areas for further research in the field of endocrine manipulation in animal production. Addressing these gaps and conducting further research in these areas will contribute to a better understanding of the effects, safety, and ethical considerations related to hormone use in animal agriculture.

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